

**A step-wise approach to a national hepatitis C screening strategy in Malaysia to meet the WHO 2030 targets: proposed strategy, coverage, and costs**

Hiebert, Lindsey; Hecht, Robert; Soe-Lin, Shan; Mohamed, Rosmawati; Shabaruddin, Fatiha; Syed Mansor, Syed Mukhtar ; Dahlui, Maznah; Azzeri, Amirah; McDonald, Scott A

*Published in:*  
Value in Health Regional Issues

*DOI:*  
[10.1016/j.vhri.2018.12.005](https://doi.org/10.1016/j.vhri.2018.12.005)

*Publication date:*  
2019

*Document Version*  
Publisher's PDF, also known as Version of record

[Link to publication in ResearchOnline](#)

*Citation for published version (Harvard):*  
Hiebert, L, Hecht, R, Soe-Lin, S, Mohamed, R, Shabaruddin, F, Syed Mansor, SM, Dahlui, M, Azzeri, A & McDonald, SA 2019, 'A step-wise approach to a national hepatitis C screening strategy in Malaysia to meet the WHO 2030 targets: proposed strategy, coverage, and costs', *Value in Health Regional Issues*, vol. 18, pp. 112-120. <https://doi.org/10.1016/j.vhri.2018.12.005>

**General rights**

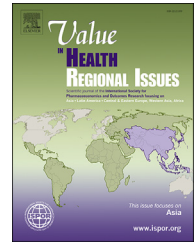
Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

**Take down policy**

If you believe that this document breaches copyright please view our takedown policy at <https://edshare.gcu.ac.uk/id/eprint/5179> for details of how to contact us.

Available online at [www.sciencedirect.com](http://www.sciencedirect.com)

ScienceDirect

journal homepage: [www.elsevier.com/locate/vhri](http://www.elsevier.com/locate/vhri)

# A Stepwise Approach to a National Hepatitis C Screening Strategy in Malaysia to Meet the WHO 2030 Targets: Proposed Strategy, Coverage, and Costs

Lindsey Hiebert, MPH <sup>1,\*</sup>, Robert Hecht, PhD <sup>1</sup>, Shan Soe-Lin, PhD <sup>1</sup>, Rosmawati Mohamed, MD <sup>2</sup>, Fatiha H. Shabaruddin, PhD <sup>3</sup>, Syed Mukhtar Syed Mansor, MD <sup>2</sup>, Maznah Dahlui, MD, MPH, PhD <sup>4</sup>, Amirah Azzeri, MBBS, MPH <sup>4</sup>, Scott A. McDonald, PhD <sup>5,6</sup>

<sup>1</sup>Pharos Global Health Advisors, Boston, MA, USA; <sup>2</sup>Department of Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; <sup>3</sup>Department of Pharmacy, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; <sup>4</sup>Centre of Population Health, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia; <sup>5</sup>Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands; <sup>6</sup>School of Health and Life Sciences, Glasgow Caledonian University, Glasgow, Scotland

## ABSTRACT

**Background:** In Malaysia, more than 330 000 individuals are estimated to be chronically infected with hepatitis C virus (HCV), but less than 2% have been treated to date. **Objectives:** To estimate the required coverage and costs of a national screening strategy to inform the launch of an HCV elimination program. **Methods:** We designed an HCV screening strategy based on a “stepwise” approach. This approach relied on targeting of people who inject drugs in the early years, with delayed onset of widespread general population screening. Annual coverage requirements and associated costs were estimated to ensure that the World Health Organization elimination treatment targets were met. **Results:** In total, 6 million individuals would have to be screened between 2018 and 2030. Targeting of people who inject drugs in the early years would limit annual screening coverage to less than 1 million individuals from 2018 to 2026. General population screening would have to be launched by 2026. Total costs were estimated at MYR 222 million (\$58 million). Proportional to coverage targets, 60% of program costs would fall

from 2026 to 2030. **Conclusions:** This exercise was one of the first attempts to conduct a detailed analysis of the required screening coverage and costs of a national HCV elimination strategy. These findings suggest that the stepwise approach could delay the onset of general population screening by more than 5 years after the program's launch. This delay would allow additional time to mobilize investments required for a successful general population screening program and also minimize program costs. This strategy prototype could inform the design of effective screening strategies in other countries.

**Keywords:** costing, elimination, hepatitis, people who inject drugs, population-level screening, screening, stepwise, targeting

© 2019 ISPOR–The professional society for health economics and outcomes research. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

### Emerging Challenges in the Elimination of Hepatitis C Virus: Finding the “Missing Millions”

Despite increasing access to and affordability of highly effective treatments for hepatitis C virus (HCV) infection, that is, direct-acting antivirals (DAAs), only 1% of infected individuals have been treated globally.<sup>1</sup> One of the emerging major challenges to

scaling up HCV treatment is the fact that only 10% of HCV chronically infected individuals have been diagnosed. The World Health Organization (WHO) HCV elimination targets call for 90% of infected patients to be diagnosed and 80% of eligible patients to be treated by 2030.<sup>1</sup> As countries strive for elimination, more than 60 million currently undiagnosed individuals will have to be identified and initiated on treatment. The effectiveness of governments and their partners to design and execute effective screening strategies to identify these “missing millions” will be a

Conflicts of interest: The authors have indicated that they have no conflicts of interest with regard to the content of this article.

\* Address correspondence to: Lindsey Hiebert, MPH, Pharos Global Health Advisors, 780 Boylston St, Apt 16J, Boston, MA 02199.

E-mail: [lindsey@pharosglobalhealth.com](mailto:lindsey@pharosglobalhealth.com)

Manuscript received June 11 2018; revised manuscript received 19 October 2018, accepted 3 December 2018.

2212-1099 - see front matter © 2019 ISPOR–The professional society for health economics and outcomes research. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<https://doi.org/10.1016/j.vhri.2018.12.005>

critical determinant of the speed with which elimination can be realized.

Despite screening being important, national HCV planning efforts can still initiate an elimination program before having a fully developed national screening strategy. In most countries, there is a pool of already diagnosed patients with HCV awaiting treatment at the launch of a national program. When countries first launch treatment campaigns, this pool of patients is usually the first to gain access, for both ethical and practical reasons. Moreover, recent examples of hepatitis treatment scale-up strategies suggest that some countries might prefer modest scale-up in the early years to allow for capacity building and resource mobilization.<sup>2</sup> As scale-up efforts move beyond the initial phase and annual treatment targets necessarily increase to keep pace with elimination ambitions, large-scale treatment programs will have to develop effective strategies to identify undiagnosed chronically infected individuals.

### HCV Context in Malaysia

In Malaysia, the HCV epidemic is a public health priority and places enormous strain on the health system. In 2009, there were an estimated 335 000 people aged 15 to 64 years living with chronic HCV infection, reflecting an estimated HCV antibody-positive prevalence of 2.5% among the adult population.<sup>3</sup> Among people who inject drugs (PWID), anti-HCV prevalence is estimated to be alarmingly high at 67%.<sup>3</sup>

Less than 2% of the estimated total infected population was treated for HCV from 2003 to 2017, about 600 patients annually in recent years.<sup>4</sup> Before 2018, patients could access DAAs only through purchasing them in the private sector or through drug trial participation. The Malaysian Ministry of Health (MMOH) announced that it would launch a national HCV treatment program in 2018,<sup>5,6</sup> following in the footsteps of other low- and middle-income countries (LMICs) that have launched large-scale DAA treatment programs, notably, Egypt, Mongolia, and Georgia. Government negotiations on DAA prices have been ongoing in Malaysia, and there have been efforts to project the HCV-related disease burden under various treatment scenarios and to estimate the treatment coverage and associated treatment costs required to meet the WHO treatment targets.<sup>7</sup> This modeling work suggests that to meet the WHO targets, 270 000 patients will have to be treated between 2018 and 2030. The total cost of patient care, management, and drug treatment was estimated at \$890 million<sup>7</sup> under one possible scale-up strategy that meets the WHO 2030 treatment targets. This scale-up begins with 5000 treated patients in 2018, increases to 20 000 annually in 2023, peaks at 30 000 from 2025 to 2028, and then falls to 25 000 per year in 2029 and 2030.

### Screening Efforts in Malaysia

Fully committing to elimination will require Malaysia to find its own missing millions. As of 2017, about 12 500 infected individuals were known to be awaiting access to DAAs and were being monitored by specialists.<sup>8</sup> The MMOH currently sponsors voluntary screening at family medicine clinics (community primary healthcare clinics) and mandatory screening at dialysis centers and blood banks. These efforts, on the basis of national hepatitis C notification data, yielded about 2000 chronic HCV cases annually before 2016 and 3000 chronic HCV cases in both 2016 and 2017 (R. Mohamed, MD, email communication, April 2018).<sup>9</sup> For PWID, annual HCV screening is a policy in opioid substitution therapy settings, but is unreliably and inconsistently enforced.

HCV screening is becoming an increasing public health priority; in 2018, several nongovernmental organizations (NGOs) launched a campaign, initially in the Klang Valley region, in collaboration with private methadone maintenance therapy

(MMT) centers, private needle and syringe exchange programs (NSPs), and family medicine specialists who volunteer to participate.

Interviews with leading clinicians, MMOH representatives, and other stakeholders have indicated that a large-scale screening program will require further decentralization of HCV screening and treatment to family medicine clinics in all states of Malaysia. Building this capacity nationwide will require major investments in human resources and training that will take years.

### Objectives

Our objectives were two-fold. We aimed to estimate both (1) the required annual screening coverage targets and (2) the cost of a national screening strategy that allow a sufficient number of patients to be identified to meet the WHO treatment targets and over time implement increasingly decentralized screening to family medicine clinics. Besides helping to inform planning efforts in Malaysia, as one of the first detailed costing exercises of a national screening program in an LMIC, our findings could serve as a prototype for other countries wishing to design screening strategies to meet the WHO HCV treatment targets.

### Methods

#### Screening Strategy Design: Stepwise Targeting

Our strategy implements decentralized general population screening to keep Malaysia on track to meet its HCV treatment goals while the capacity and resources for widespread screening at family medicine clinics are mobilized. Baseline screening activities serve as the foundation for this screening strategy. The initial phase prioritizes targeting of PWID to delay the onset of decentralized, general population screening and achieve programmatic efficiency, because efforts to screen this high-prevalence population within MMT programs are already underway. PWID belong to the largest high-risk group for HCV in Malaysia and were subsequently divided into the following subgroups: current MMT clients, current and former NSP clients, relapsed MMT clients, other active PWID, and former PWID. In the final phase, intensive general population screening at family medicine clinics kicks off after there are no longer enough infections among PWID to yield enough treatment-eligible individuals to meet targets. In our proposed strategy, general population screening represents the scale-up of active screening efforts in family medicine clinics where family medicine specialists would use a short questionnaire to “pre-screen” for high-risk behaviors. We called this strategy the “stepwise” approach (see Fig. 1).

#### Calculating Screening Coverage

Screening coverage was reverse-calculated along the cascade of care from a required yield to sufficiently meet annual treatment targets. Figure 2 illustrates the calculation process. For baseline screening activities that were assumed to produce a constant screening yield, the number of filled treatment spots was determined after accounting for effective linkage to care, or the percentage of the screening yield successfully initiated on treatment. Then, the required screening yield from PWID targeting and general population screening to fill the remaining treatment spots was calculated, after again accounting for linkage to care. For the treatment targets to be met, at least 55% linkage to care among PWID and 80% linkage to care among the general population would be required (see [Supplemental Materials](https://doi.org/10.1016/j.vhri.2018.12.005) found at <https://doi.org/10.1016/j.vhri.2018.12.005>). For estimates lower than these, all eligible persons would be

Year	18	19	20	21	22	23	24	25	26	27	28	29	30	
<b>1. Baseline screening</b>														Baseline screening efforts represent ongoing HCV screening activities.
Known patients														Known patients have been diagnosed previously and are being actively monitored by clinicians
Existing Ministry screening program														Established Ministry screening programs in Malaysia include initiatives in dialysis centers and blood banks, as well as select family medicine clinics
Opportunistic screening														Opportunistic screening at tertiary hospitals will continue to occur among patients that present with symptoms of advanced liver disease
New 2018 campaign														The 2018 campaign focuses on screening of high-risk populations at MMT, NSP, and select family medicine clinics. This campaign will be absorbed by PWID screening when launched and the ongoing efforts at family medicine clinics would be captured under the "existing program."
<b>2. PWID targeting</b>														The PWID population was defined to include both former and active injection drug users since former users would have previously had high exposure to HCV. PWID were divided into the five sub-groups below:
Current MMT clients														Current MMT clients are actively adhering to methadone maintenance therapy. Annual HCV screening is currently required at MMT clinics but not enforced.
Active and former NSP clients														Both active and former needle and syringe exchange clients would be targeted together, considering the social network dynamics of needle and syringe exchange users.
Relapsed MMT Clients														These MMT clients are no longer adhering to methadone maintenance therapy. However, these individuals are known to MMT clinics.
Other active PWID														These individuals are active PWID who are not currently linked to MMT or NSP and have not previously received services. New platforms to reach this group will be required.
Former PWID														These individuals are no longer active PWID but have a high HCV prevalence due to previous exposure. New platforms to reach these PWID will be required.
<b>3. General population screening:</b>														Individuals to be screened in family medicine clinics represent the remaining undiagnosed population who have likely acquired HCV through medical or community transmission routes (blood transfusions, nosocomial infections, piercings, tattoos, etc) and are unaware of their risk for chronic HCV infection.
High-risk screening in general population														

Fig. 1 – “Stepwise” screening approach schematic.

screened, but too few would be linked to treatment. From the required yield for each baseline activity or subgroup, confirmatory test coverage was determined after factoring in the prevalence of chronic infection status among persons anti-HCV positive, which determines treatment eligibility and is informed by confirmatory HCV core antigen testing. From required confirmatory test coverage, anti-HCV test coverage was determined after accounting for the prevalence of anti-HCV in the subpopulation, which is informed by anti-HCV testing. HCV core antigen

testing was selected because it is currently the cheapest confirmatory test option in Malaysia. The prevalence of chronic infection status was assumed to be identical across all groups. Unique estimates of anti-HCV prevalence were used for subgroups. Key assumptions on anti-HCV prevalence, chronic infection status, and linkage to care are presented for each subgroup in Table 1.

Herein we provide further assumptions on how the coverage estimates were calculated using the stepwise approach.

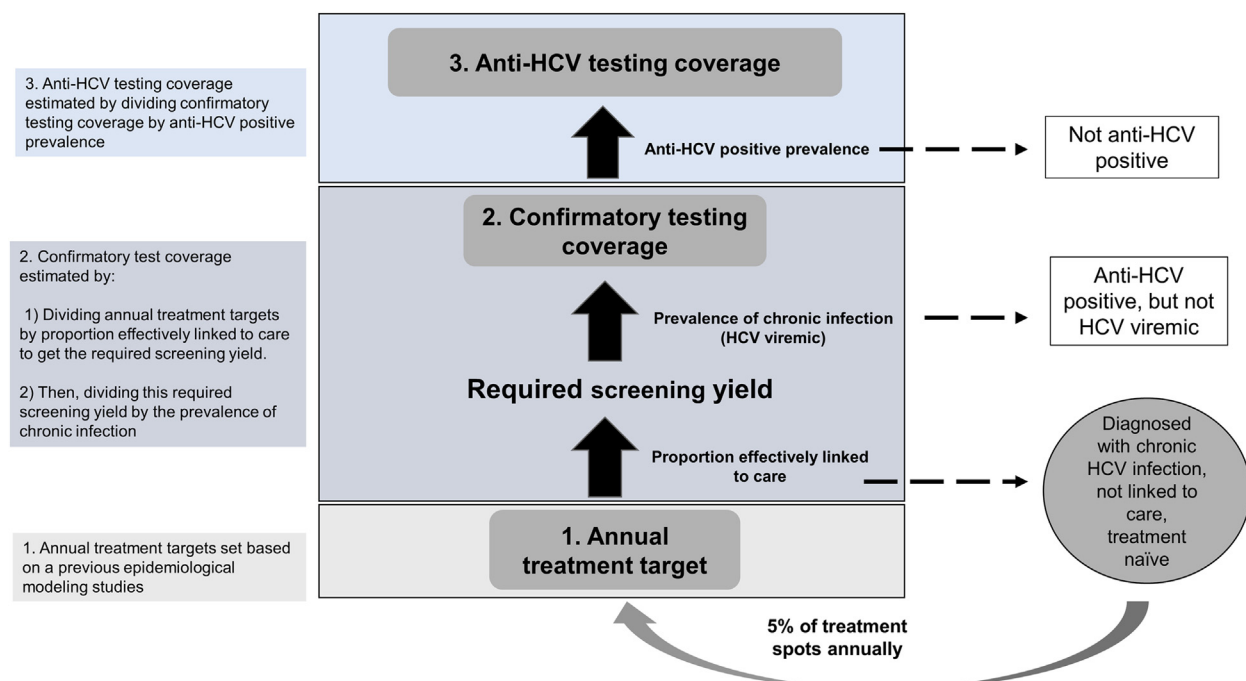


Fig. 2 – Screening coverage calculation process diagram. HCV indicates hepatitis C virus.

**Table 1 – Assumptions regarding anti-HCV prevalence, chronic infection status, and linkage to care for each population subgroup.**

Subgroup	Anti-HCV prevalence	Chronic infection status*	Linkage to care	Total population size
<i>Baseline screening activities</i>				
Known patients	100%	100%	100%	12 500 <sup>8</sup>
Existing Ministry of Health screening efforts at dialysis centers, blood banks, and family medicine clinics	10% <sup>†</sup>	74% <sup>16</sup>	80%	Unknown but assumed notification rate of 3000 annually remains constant <sup>†</sup>
Opportunistically screened by specialists (inpatient)	100%	74% <sup>16</sup>	80%	Assumed that 5% of treatment spots would be filled by those opportunistically screened annually
Anticipated 2018 campaign	63.1% <sup>17</sup>	74% <sup>16</sup>	55%	18 000 <sup>17</sup>
<i>PWID targeting</i>				
Current MMT clients	63.1% <sup>17</sup>	74% <sup>16</sup>	55%	18 000 <sup>17</sup>
Current and former NSP clients	67.1% <sup>3</sup>	74% <sup>16</sup>	55%	85 170 <sup>15,17,‡</sup>
Relapsed MMT clients	67.1% <sup>3</sup>	74% <sup>16</sup>	55%	30 000 <sup>15,17,§</sup>
Other active PWID	67.1% <sup>3</sup>	74% <sup>16</sup>	55%	36 830 <sup>17,  </sup>
Former PWID	67.1% <sup>3</sup>	74% <sup>16</sup>	55%	229 200 <sup>3,¶</sup>
<i>General population screening</i>				
Adult population	2.5% <sup>3</sup>	74% <sup>16</sup>	80%	18.1 million <sup>3</sup>
High-risk groups in general population	2.9% <sup>£</sup>	74% <sup>16</sup>	80%	6.4 million <sup>£</sup>
Delayed linkage to care population	100%	100%	100%	This subgroup consists of all those who are not successfully linked to care across subgroups. This subgroup continues to grow over time and 5% of treatment targets are assumed to be filled from delayed initiators.

HCV, hepatitis C virus; MMT, methadone maintenance therapy; NSP, needle and syringe exchange program; OST, opioid substitution therapy; PWID, people who inject drugs.

\* Chronic infection status represents the prevalence of chronic infection among anti-HCV positive individuals.

<sup>†</sup> Based on personal communication with R. Mohamed, MD (email communication, April 2018).

<sup>‡</sup> On the basis of the Global AIDS Progress Report 2016,<sup>13</sup> 85% of PWID were reached through OST and NSP and 35% were reached through MMT only. Therefore, approximately 50% of the 170 000 active PWID were assumed to be reached only by NSP.

<sup>§</sup> On the basis of the Global AIDS Progress Report 2016,<sup>13</sup> there are 10 000 new MMT clients annually. About 30% of these clients, or 3000, relapse annually.<sup>14</sup> Over 10 years, this population size will grow to about 30 000 (assuming 3000 times 10).

<sup>||</sup> This figure was calculated as the number of remaining active PWID not in MMT and NSP programs, assuming there is a total of 170 000 active PWID.<sup>13</sup>

<sup>¶</sup> This figure was calculated as the remaining PWID population, assuming that the total current and former PWID population is 399 200.<sup>3</sup>

<sup>£</sup> Calculated from the assumption of 144 312 non-PWID chronically HCV-infected persons, on the basis of 41% of total chronically HCV-infected persons being non-PWID.<sup>3</sup> The approximate population size of the high-risk groups within the general population was calculated after assuming a 2.9% anti-HCV prevalence and chronically infected status of 74% among individuals anti-HCV positive.<sup>17</sup> The highest prevalence reported among risk sex/ethnicity strata in Malaysia was 2.9%.<sup>3</sup> See [Supplemental Materials](#) for additional information.

### Baseline screening activities

- **Known patients:** The backlog of known patients was assumed to be treated in the first 3 years of the program. It was assumed that no additional screening of already known patients would be needed.
- **Existing MMOH program:** The existing MMOH screening program at dialysis centers, blood banks, and a limited number of family medicine clinics was assumed to yield 3000 chronic HCV cases annually until 2023, on the basis of the estimated yield in 2017 (R. Mohamed, MD, email communication, April 2018). It was assumed that after 2023, this yield would decline to 1000 chronic HCV cases annually by 2027 as the other active screening initiatives were expanded.
- **Opportunistic screening:** Opportunistic screening among patients with advanced liver disease in tertiary care centers was assumed to yield 5% of the required treatment coverage annually in the early years, with this percentage decreasing to 2% over time, because active screening efforts would kick in and

more patients would be diagnosed before the onset of serious complications.

- **2018 screening campaign:** It was assumed that the screening campaign launched in 2018 will yield 500 chronic HCV cases annually (R. Mohamed, MD, email communication, April 2018).

From these yields, the required anti-HCV and confirmatory test coverage was then calculated.

### PWID targeting

Once the annual national treatment targets became larger than the yield from baseline activities, PWID targeting was initiated to fill the gap. The remaining number of treatment spots to be filled was determined after accounting for baseline activities, and then the associated yield and anti-HCV and confirmatory test coverage required were calculated as described previously. The NGO campaign launched in 2018 working with private MMT and NSP centers was assumed to be absorbed by scaled-up PWID targeting



efforts. To avoid overstretching outreach efforts, PWID targeting focused on one subgroup at a time (ie, current MMT clients, NSP clients, relapsed MMT clients, other active PWID, and finally former PWID). After full coverage of one subgroup was reached, the next subgroup was targeted.

### General population screening

After PWID targeting no longer yielded a sufficient number of patients to meet the annual national targets to reach elimination by 2030, general population screening filled any remaining annual treatment gaps. The number of treatment spots to be filled was determined after accounting for baseline screening and PWID targeting. The required screening yield for these spots and associated anti-HCV and confirmatory test coverage were calculated as described previously.

To account for those individuals who were unsuccessfully linked to care after being diagnosed, 5% of the ever-screened but treatment-naïve pool was assumed to initiate treatment each year. Individuals from all subgroups contributed to this pool. No data were available to inform this estimate, but we applied a conservative approximation of 5% to avoid underestimating the required additional screening each year from other subgroups. Because the individuals in this pool had already been screened, additional screening costs were not incurred.

It was assumed that sensitivity and specificity of anti-HCV testing would be close to 100%, as indicated in the WHO guidelines.<sup>10</sup> It was also assumed that all individuals who were offered screening would give consent.

### Calculating Screening Costs

Direct screening costs consisted of variable costs for screened individuals and fixed program costs for capacity building. Total variable costs were estimated by determining a cost per anti-HCV test and HCV confirmatory test administered, and multiplying by the relevant coverage estimates for each test. The cost per anti-HCV test included the unit cost of the anti-HCV test kit and service delivery. The cost per confirmatory diagnosis included the unit cost for an HCV core antigen test and service delivery. Service delivery costs were collected for PWID and other non-PWID subgroups separately (baseline screening, general population, etc), because delivery platforms differ significantly. Unit costs are presented in [Table 2](#). Costs of liver disease staging were excluded.

Program costs for capacity building and demand generation were also included, specifically for healthcare training and national awareness campaigns at MYR 3.2 million per year (~\$1 million). No national strategy exists for Malaysia, but benchmarks based on strategic plans from other countries were used.<sup>2</sup>

Future costs were inflation-adjusted according to a rate of 2.5%. Costs are presented in both Malaysian ringgit and US dollars. The exchange rate on April 3, 2018 (1 MYR = \$0.26) was used.

### Sensitivity Analysis

Estimates of linkage to care, the proportion of chronically infected persons who begin treatment following diagnosis, in Malaysia are highly uncertain. Some estimates exist for when interferon was the standard of care (A. Azzeri et al, unpublished data, 2018), but no data on linkage to care are available for the DAA era. Because of lack of data on this proportion, a sensitivity analysis was conducted on the linkage to care proportion for both PWID and the general population. Specifically, we calculated the total coverage requirements and total costs for a 5% increase in the baseline linkage to care proportions to demonstrate the sensitivity of the total coverage and cost estimates to this parameter. Sensitivity to less effective linkage to care estimates was not explored because the baseline linkage to care proportions represent the minimum

**Table 2 – Unit cost assumptions.**

Unit cost	Outpatient settings (MYR/\$)	MMT settings (MYR/\$)
Total cost per anti-HCV test delivered	15.5/3.8	52.5/12.8
Anti-HCV test	2.5/0.6*	2.5/0.6*
Service delivery	13.0/3.2 <sup>18</sup>	50.0/12.2 <sup>19</sup>
Total cost per HCV core antigen test delivered	62.0/15.1	99.0/24.1
HCV core antigen test	49.0/11.9*	49.0/11.9*
Service delivery	13.0/3.2 <sup>18</sup>	50.0/12.2 <sup>19</sup>

HCV indicates hepatitis C virus; MMT, methadone maintenance therapy.

\* Based on personal communication with R. Mohamed, MD (email communication, April 2018).

values required to meet the 2030 targets. See [Supplemental Materials](#) for further details.

### Data Sources

Authors received permission to use data from sources involving personal communications. All calculations were carried out in Microsoft Excel. See [Supplemental Materials](#) for more information on data sources.

## Results

### Screening Coverage

In total, 6 million people would need to be screened between 2018 and 2030 under the stepwise strategy to meet the WHO treatment targets. Relying on baseline screening efforts and PWID targeting would result in a lower required screening coverage in the early years. In 2018, year one at the time of the analysis, the total anti-HCV test coverage required to treat 5 000 individuals would be approximately 42 000. In 2024, the total number of individuals to be screened would be approximately 105 500 to yield 25 000 individuals initiated on treatment. General population screening would have to be rolled out in 2026 to supplement PWID screening activities, and by 2027 the required number of patients to be screened annually would increase to more than 1.4 million to yield 30 000 individuals initiated on treatment.

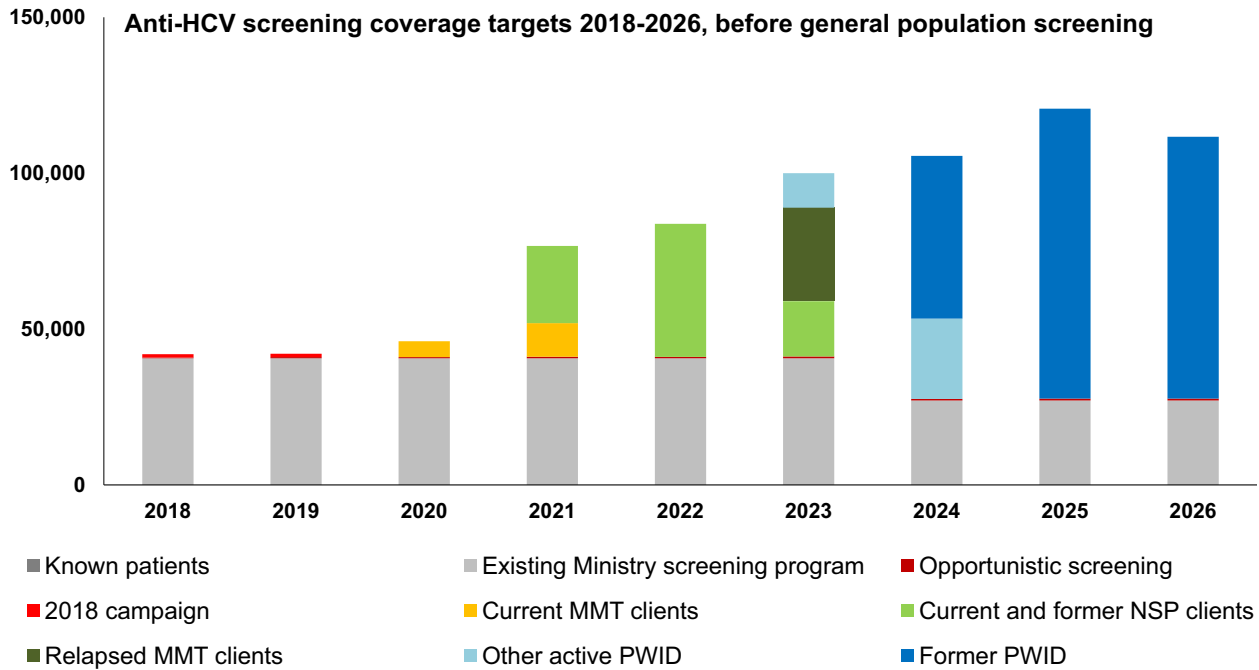
We describe herein the anti-HCV screening coverage required within each phase of the program. Annual coverage requirements for each subgroup for both anti-HCV and confirmatory testing can be found in the [Supplemental Materials](#).

### Baseline screening activities

The pool of 12 500 known patients would be treated in the first 3 years, but these patients would not add to the required screening coverage in those years. Existing MMOH screening programs would continue screening about 40 600 patients each year, and the 2018 campaign would screen 1073 patients annually until 2020, when targeted PWID screening would begin.

### People who inject drugs

Starting in 2020, baseline screening would no longer yield enough treatment-eligible persons to stay on pace with treatment targets. PWID screening coverage would have to increase from about 5069 current MMT clients in 2020 to reaching 93 015 former clients in



**Fig. 3 – Anti-HCV screening coverage targets 2018-2026, before general population screening.** HCV indicates hepatitis C virus; MMT, methadone maintenance therapy; NSP, needle and syringe exchange program; PWID, people who inject drugs.

2025. Figure 3 illustrates the number of persons in each PWID subgroup to be screened from 2018 to 2026.

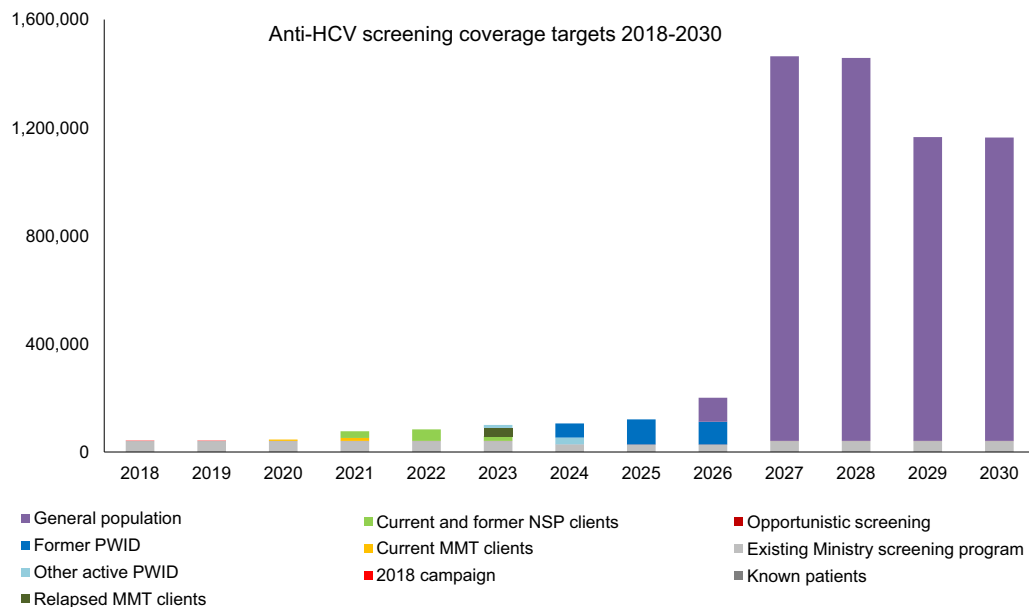
#### General population screening

The stepwise strategy would effectively delay the onset of general population screening until 2026. Because of the lower anti-HCV prevalence in the general population, total anti-HCV test coverage would spike to more than 1.4 million individuals per year in 2027 to 2028 before dropping slightly to 1.2 million individuals per year in 2029 to 2030. In all, about 90% of the total individuals to

be screened would fall in the period 2026 to 2030. Figure 4 shows required screening coverage for all subgroups, including among the general population, for 2018 to 2030.

#### Estimated costs

The total cost of the national screening program was estimated at MYR 222 million (\$58 million). Annual costs were projected to increase from MYR 3.9 million (\$1.0 million) in 2018 under baseline screening efforts to MYR 9.5 million (\$2.5 million) in 2025 under PWID targeting. The costs were projected to reach MYR 31.6



**Fig. 4 – Anti-HCV screening coverage targets 2018-2030.** HCV indicates hepatitis C virus; MMT, methadone maintenance therapy; NSP, needle and syringe exchange program; PWID, people who inject drugs.

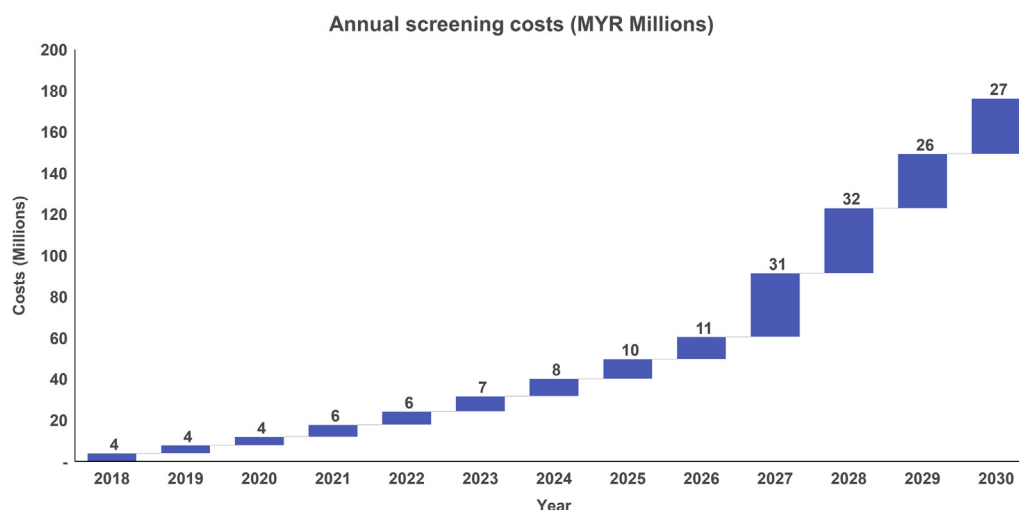


Fig. 5 – Annual screening costs 2018–2030.

million (\$8.2 million) in 2028, the peak of the general population screening effort (Fig. 5).

### Sensitivity Analysis

The total cost of the screening program was sensitive to the linkage to care parameters. If the linkage to care proportion for the PWID or the general population dropped even 5% below baseline values, then the WHO treatment target could not be achieved by 2030, because an insufficient number of patients would be initiated on treatment annually to sustain treatment targets.

If linkage to care proportions increased by 5%, then the screening program would become less costly. For instance, if the proportion linked to care after general population screening improved from 80% to 85%, the total required number of total anti-HCV screening coverage would be reduced to 5.6 million individuals—which is 0.4 million fewer than baseline—and the total cost of the program would drop to MYR 214 million (\$56 million), which is about 4% less than baseline. Nevertheless, if linkage to care among PWID improved from 55% to 60%, total anti-HCV screening coverage requirements and total program cost would be similar to baseline, at 6 million individuals and MYR 220 million (\$57 million). General population linkage to care had a greater influence on total coverage and costs because general population screening accounts for more than 90% of the required screening coverage.

### Discussion

This study is one of the first attempts to conduct an in-depth analysis of the required screening coverage and estimated costs of a national HCV elimination strategy. Although other studies have discussed the costs and benefits of universal screening for HCV, particularly in the United States and early adopting LMICs,<sup>11–14</sup> we have put forward a targeted stepwise approach that demonstrates how targeted screening can give countries more time to scale up a decentralized general population screening program.

This stepwise approach indicated that a general population screening program would not be required immediately to stay on pace for elimination by 2030, and that targeting of high-risk subgroups could sustain progress toward meeting elimination treatment targets for more than 5 years. This delay would provide a

vital window of time for the operational capacity of a decentralized program to be developed. Malaysia's existing baseline screening efforts are expected to be strong enough to sustain progress toward treatment targets until 2020. In 2020, additional screening scale-up would be needed, and we demonstrated that by targeting PWID in the early years, more extensive general population screening efforts could be delayed. After 2025, there would be too few infected PWID to meet treatment targets, and screening of the general population would ultimately have to kick in to meet the WHO 2030 treatment targets.

In total, 6 million individuals would need to be screened—about one-fifth of Malaysia's current total population. At the peak of the program, in the later years (2027–2030), about 1.2 to 1.4 million individuals would have to be screened each year. Although large, this number appears feasible given that the established Malaysian HIV/AIDS program screened 1.4 million individuals in 2014,<sup>15</sup> and that MMOH would have about 8 years from the time of writing this paper to prepare the HCV program to reach these HIV screening levels. Currently, HIV screening is compulsory at premarital registration and is routinely done for antenatal checkups.

The targeted stepwise approach would not only address operational and capacity constraints by delaying general population screening in the early years but also help minimize overall screening costs during this period. Targeted PWID screening is more efficient than general population screening because of the greater yield per given number of individuals screened. In Malaysia, the prevalence of HCV is estimated to be more than 20 times higher in PWID than in general population adults,<sup>3</sup> which implies that fewer PWID have to be screened to find one individual eligible for treatment compared with members of the general population.

If the stepwise approach is not adopted, and instead general population screening is initiated from the start, approximately 7 million additional patients would need to be screened through 2030 with a total program cost estimated at MYR 317 million (\$82 million). Thus, the stepwise screening strategy would be 40% less costly, or save MYR 95 million (\$24 million) compared with a strategy that immediately adopts widespread general population screening.

The current findings highlight the reality that an elimination screening program will require substantial investment, and that strategic planning for screening cannot be placed on the back burner. At current expected DAA prices, screening costs represent



about 7% of total patient care, management, and drug treatment costs, which have been estimated at MYR 3.6 billion (\$890 million) for a treatment scale-up scenario adequate to meet the WHO 2030 targets.<sup>7</sup> As drug prices continue to drop on the basis of global trends,<sup>1</sup> screening will represent a growing proportion of the overall HCV program cost. Efficiencies in screening test manufacturing, procurement, and service delivery should be identified to potentially lower the costs of the program.

An important secondary finding from this analysis is that if linkage to care is poor, it will be impossible to meet the annual treatment targets for elimination. The obtained linkage to care proportion thresholds were 55% for PWID and 80% for the general population. This finding highlights the need for supportive policies and initiatives that lead to improved case-finding, referral to care, and initiation of therapy, as well as good rates of adherence to treatment. There is limited existing evidence regarding effective interventions to improve linkage to care, but demonstration studies are ongoing and these findings must be used to evaluate the possible utility of solutions such as linkage workers or incentive programs to promote both high rates of initial linkage to care and long-term follow-up. The model results assumed that delayed linkage to care is possible, suggesting that antiviral therapy can be initiated at a later date for those patients who do not wish or are not able to begin treatment immediately.

Our analysis points to additional HCV policy research priorities. For instance, it may be beneficial to integrate screening projections into a more advanced dynamic HCV transmission model to incorporate projected changes in prevalence over time. Our tool may have underestimated the coverage and costs required in the later years of the program, when chronic HCV prevalence among all subgroups is expected to decrease. We implicitly assumed that potential decreases in prevalence would be offset by other—unaccounted for—factors that have an effect in the opposite direction, including potential price reductions in anti-HCV tests and improved linkage to care as the program matures. We did not model possible growth of infected PWID subpopulations and reinfection, but we also did not account for mortality in the PWID population and this would partially balance out any observed growth. Moreover, we did not account for individuals who wish to decline screening, but we recognize that all individuals have the autonomy and right to informed consent and could decline HCV screening when offered by a clinician. Looking forward, HCV screening tools could also be improved to capture more of the complexity of HCV screening and treatment dynamics, including population growth, reinfection of PWID, the benefits of treatment as prevention, and consent.

The robustness of our coverage and cost estimates is also limited by the quality of evidence that exists for current linkage to care and the effectiveness of the cascade of care. A number of the assumptions underlying our results are based on unpublished sources, such as communications with clinicians and government reports. In the absence of further validated estimates, the estimates used in this article represent the best data for initiating discussion around this important HCV policy topic. Additional data collection, including updated seroprevalence studies, size estimation of key populations, and evaluation of the level of linkage to care achieved in the various subgroups should be conducted.

This work represents an initial exercise to guide screening strategy development in Malaysia. The main findings could be used to plan and prepare for targeted screening of PWID starting in the next few years and a general population-level program at the primary care level in full effect about five years later, but there are still details to be worked through if this strategy were to be operationalized. Active PWID are very accessible in one sense, because many already have contact with civil society organizations and health facilities through NSP and MMT programs.

Nevertheless, how HCV screening will be integrated into current services in a consistent way remains to be determined, and how former drug users and other active users who do not interact with these programs will be reached requires further discussion with community stakeholders. A general population screening program that covers more than a million people annually cannot be launched overnight. Extensive discussion among Ministry of Health officials, hepatologists, NGOs, and other stakeholders will be required to address how resources from targeted screening could be transferred to a general population screening program and what other steps could be taken to prepare for this buildup and successful decentralization. Finally, the means by which the proposed screening strategy can fit within a longer term screening strategy beyond 2030 will also have to be addressed.

We suggest that similar exercises estimating the coverage and cost of HCV screening should be conducted in other countries that are considering launching national HCV elimination programs. In these settings, this exercise will assist in improving the understanding of the resources required and the implications of the proposed screening strategy in terms of resource mobilization, healthcare training, and other enabling activities. It is likely that a stepwise strategy is practical only in a setting with an epidemiological context with a significant burden among PWID, but each country context will have to be fully evaluated.

## Conclusions

Finding the missing millions is a daunting challenge in HCV elimination. Investment in a national screening program is crucial; without effective identification of chronically infected individuals, it will be impossible to meet treatment targets. Because both financial and operational challenges can easily impede screening efforts, it will be important to ensure that efficient, cost-minimizing screening strategies are thoughtfully designed and executed. These findings will be useful for informing the planning and launching of a large-scale national HCV screening strategy in Malaysia. We hope this analysis will also serve as a prototype that can aid other countries in the design and implementation of national HCV screening programs.

## Acknowledgments

We thank the Ministry of Health for originally inviting us to conduct this analysis and for providing the required data when available. We are grateful for the feedback of Dr Adeeba Kamarulzaman on early findings.

Source of financial support: This study was supported by a grant from Gilead Sciences. The authors were in no way influenced by this funding source.

## Supplemental Materials

Supplementary data associated with this article can be found in the online version at <https://doi.org/10.1016/j.vhri.2018.12.005>.

## REFERENCES

1. World Health Organization. *Global Hepatitis Report 2017*. Geneva, Switzerland: World Health Organization; 2017.
2. Hecht R, Hiebert L, Spearman W, et al. The investment case for hepatitis B and C in South Africa: adaptation and innovation in policy analysis for disease program scale-up. *Health Policy Plan*. 2018;33(4):528–538.

3. McDonald SA, Mohamed R, Dahlui M, et al. Bridging the data gaps in the epidemiology of hepatitis C virus infection in Malaysia using multi-parameter evidence synthesis. *BMC Infect Dis.* 2014;14:564.
4. Mohamed R. Hepatitis C modeling in Malaysia—meeting the 2020 and 2030 targets. Oral presentation at National Viral Hepatitis Meeting, Kuala Lumpur, Malaysia; January 2017.
5. Director General of Health, Ministry of Health Malaysia. Press statement DG of health 29th July 2017—Walk-a-run hepatitis 2017. <https://kpkesihatan.com/2017/07/29/press-statement-dg-of-health-29th-july-2017-walk-a-run-hepatitis-2017/>. Accessed April 3, 2017.
6. Director General of Health, Ministry of Health Malaysia. Press statement Minister of Health 20th September 2017—implementation of the rights of government for sofosbuvir tablet to increase access for hepatitis C treatment in Malaysia. <https://kpkesihatan.com/2017/09/20/press-statement-minister-of-health-20th-september-2017-implementation-of-the-rights-of-government-for-sofosbuvir-tablet-to-increase-access-for-hepatitis-c-treatment-in-malaysia/>. Accessed April 3, 2017.
7. McDonald SA, Azzeri A, Shabaruddin FH, et al. Projections of the healthcare costs and disease burden due to hepatitis C infection under different treatment policies in Malaysia, 2018–2040. *Appl Health Econ Health Policy.* 2018;16(6):847–857.
8. Jahis R. National strategic plan for viral hepatitis: towards 2030's goal. Oral presentation at National Viral Hepatitis Meeting, Kuala Lumpur, Malaysia; January 2017.
9. Ministry of Health Malaysia. *National Strategic Plan on Viral Hepatitis 2017–2030* [draft document]. Kuala Lumpur, Malaysia: Ministry of Health; 2017.
10. World Health Organization. *Guidelines on Hepatitis B and C Testing*. Geneva, Switzerland: World Health Organization; 2017.
11. Assoumou SA. Cost-effectiveness of one-time hepatitis C screening strategies among adolescents and young adults in primary care settings. *Clin Infect Dis.* 2018;66(3):376–384.
12. Nasrullah M, Sergeenko D, Gvinjilia L, et al. The role of screening and treatment in national progress toward hepatitis C elimination—Georgia, 2015–2016. *MMWR Morb Mortal Wkly Rep.* 2017;66(29):773–776.
13. Reilley B, Leston J, Hariri S, et al. Birth cohort testing for hepatitis C virus—Indian Health Service 2012–2015. *MMWR Morb Mortal Wkly Rep.* 2016;65(18):467–469.
14. Kim DD, Hutton DW, Raouf AA, et al. Cost-effectiveness model for hepatitis C screening and treatment: implications for Egypt and other countries with high prevalence. *Global Public Health.* 2015;10(3):296–317.
15. HIV/STI Section, Disease Control Division, Ministry of Health Malaysia. Global AIDS response progress report. 2016. [http://www.moh.gov.my/images/gallery/Report/Malaysia%20GARPR%202016\\_Final.pdf](http://www.moh.gov.my/images/gallery/Report/Malaysia%20GARPR%202016_Final.pdf). Accessed April 30, 2018.
16. Micallef JM, Kaldor JM, Dore GJ. Spontaneous viral clearance following acute hepatitis C infection: a systematic review of longitudinal studies. *J Viral Hepat.* 2006;13(1):34–41.
17. Norsiah A, Salina A, Salmah N, et al. *Malaysian Methadone Treatment Outcome Study (MyTOS)*. Kuala Lumpur, Malaysia: Ministry of Health Malaysia; 2016.
18. Yong YV, Shafie AA. How much does management of an asthma-related event cost in a Malaysian suburban hospital? *Value Health Reg Issues.* 2018;15:6–11.
19. Disease Control Division, Ministry of Health Malaysia. *Methadone Program in Malaysia Unit Costs*. Kuala Lumpur, Malaysia: Ministry of Health Malaysia; 2017.